

VICH Biological Quality Monitoring WG
Topic: Residual Moisture Testing

Collaborative Study Protocol

Performance Characteristic Determination
Gravimetric Method for Residual Moisture
Proposed VICH Guideline

Purpose:

To determine the performance characteristic of the VICH proposed gravimetric test for residual moisture as conducted by industry and government reference labs in Japan, Europe, the United States and observer countries.

Testing plan overview:

Determining the performance characteristics of the proposed gravimetric test for residual moisture will take place in two phases. The first phase of the study will consist of the distribution of samples composed of a desiccated stabilized reference lactose to the three regions. These standards will be prepared as single (1ml) and 10 dose (10 ml) sizes.

A maximum of 5 industry and government labs from each region (EU/US/Japan and official observer) will be selected by the WG representatives to participate in this study. Each participating lab will test the samples by their current assay and VICH gravimetric assay. Results will be collected by the regional government lab and submitted to the topic leader. These data will show the consistency of testing between regions over a range of residual moisture levels and products.

Phase two would involve the evaluation of a minimum of 5 regional products, in duplicate, using their current regional assay and the VICH gravimetric assay. These data will demonstrate the utility of the guideline assay for a variety of products, and provide preliminary data the consistency of the assay over a variety of products.

Materials and Methods:

Test Articles, phase 1: Samples have been prepared from desiccated reference lactose (Sigma lot 00-0474-00) for distribution. Vials are labeled for in-vitro use only. The lactose solution was autoclaved prior to dispensing.

Government labs will be responsible for obtaining import permits. The USDA will be responsible for sample distribution to the Japan Government Lab and to the EP. The Japan Government Lab and the EP will be responsible for distribution to industry participants.

Current standard procedure: Collaborators will also conduct tests according to their standard moisture method. They will provide details of the test procedure along with the results. Labs currently running Gravimetric Assay can provide that data only. Any variances in test procedure from the proposed VICH guideline should be identified.

Collaborative Instructions:

Detailed instructions will be distributed with the collaborative samples, including: names and addresses of coordinators, instructions on methods, checklists, reporting forms, and other information.

Results:

All results should be reported to the region (or observer) coordinating lab. From there, results will be forwarded to the topic leader for analysis and reporting

Timeline:

March 21, 2000	WG forwards draft protocol to WG members
April 1, 2000	USDA distributes collaborative samples and materials through coordinators
May 26, 2000	Collaborators complete all testing and report
June 2, 2000	Data analysis completed
June 9, 2000	Report of study results to members
July 11-14, 2000	WG meeting

Appendix 1: Residual Moisture Assay

1. Materials and equipment

- 1.1 Cylindrical weighing bottles--individually numbered with airtight glass stoppers.
- 1.2 Vacuum oven--equipped with validated thermometer and thermostat. A suitable air-drying device must be attached to the inlet valve.
- 1.3 Balance--capable of accurate readability to 0.1 mg (rated precision ± 0.01 mg).
- 1.4 Desiccator--with phosphorus pentoxide, silica gel or equivalent
- 1.5 Sample--desiccated veterinary vaccine in original sealed vial.

2. Preparation for the test

2.1 Preparation for the test--weighing bottles

Label the weighing bottle for **sample**(s). Thoroughly clean weighing bottles. Place stopper at approximately a 45° angle on top of bottle and dry for a minimum of 30 minutes at $60^{\circ} \pm 3^{\circ}\text{C}$ under vacuum (<2.5 kPa). While hot, immediately transfer bottles and stoppers into a desiccator. Allow to cool to room temperature, close stopper, weigh and record the weights (to nearest 0.1 mg.) as "A". Return bottles to desiccator.

2.2 Preparation of the sample and the control

Retain sample and control, in original airtight containers at room temperature until use. Do not break the seal until ready to proceed.

2. Performance of the test

2.1 Procedure

- 2.1.1 Break sample container seal. Using a spatula, break up desiccated product and rapidly transfer (minimum of 100 mg, 50 mg for single dose products, use more than one vial for single dose products if needed) to a previously weighed bottle. Close stopper and immediately weigh. Record the weight as "B".
- 2.1.2 Place the bottle with the stopper at approximately a 45° angle in the vacuum oven. Set vacuum to <2.5 kPa and the temperature to $60^{\circ} \pm 3^{\circ}\text{C}$.
- 2.1.3 After 3 hrs, turn off the vacuum pump and bleed dry air into the oven until the pressure inside of the oven is equalized with the atmosphere.
- 2.1.4 While the bottle is still warm, leave the stopper at angle, transfer to desiccator, and allow to cool to room temperature (more than 2 hr). Close stopper, weigh, and record the weight as "C".

2.2 Calculations

Record weights

A is tare weight of bottle.

B minus A is weight of sample before assay.

B minus C is weight equivalent to residual moisture of sample.

Then $((B - C) / (B - A)) \times (100) = \% \text{ of residual moisture.}$

4. Results

Results are considered satisfactory if per cent residual moisture is less than or equal to the manufacturer's specification